

The Effects of Cold-Stored Platelets on Hemorrhagic Patients: A Meta-Narrative Review

Cynthia Medina*, Vivian Nguyen*, Kim Pham*, Pham Vu*, Mary Coolbaugh-Murphy, Ph.D., MB(ASCP)^{CM}, Denise M. Juroske Short, Ph.D., MB(ASCP)^{CM}

Clinical Laboratory Science Program, School of Health Professions, UT MD Anderson Cancer Center

* Authors contributed equally and are listed in alphabetical order

Introduction

Platelet transfusions became prevalent in the 1960s when they started being used as an alternative to whole blood transfusions. They are commonly used to treat patients with thrombocytopenia, platelet disorders, and actively bleeding patients. Room temperature platelets (21-24° C) have a 7-day shelf life, while cold-stored platelets (1-6° C) have a 14-day shelf life (Center, 2023). Room temperature platelets (RTP) have a better hemostatic activity than cold-stored platelets (CSP) post transfusion, however, cold storage platelets can be stored for longer use, there's a reduction in bacterial growth, and a reduced risk of transfusion reactions. Despite this, the use of CSP were quickly abandoned soon after due to the platelet's short circulation time in the blood after transfusion (Mack, 2020). Although the platelets were absent 24 hours after transfusion, this makes it optimal for emergency use (George, 2023). The peak interest for CSP re-emerged due to them being more accessible and having a longer shelf life, making it easier to transfuse in actively bleeding cases. Currently, the FDA has approved it for use in active bleeding cases to maintain levels of platelet inventory. Research of CSP has compared the advantages of CSP to RTP to provide a solution to the on-going platelet inventory shortage problem. This research can have a positive effect to see if CSPs could possibly be used for prophylactic transfusions and RTPs for therapeutic purposes.

Figure 1. Introduction and Fast Approach of Cold-Stored Platelets



Note: This picture depicts how useful and fast cold-stored platelets can be deployed in emergency situations.

Research Question

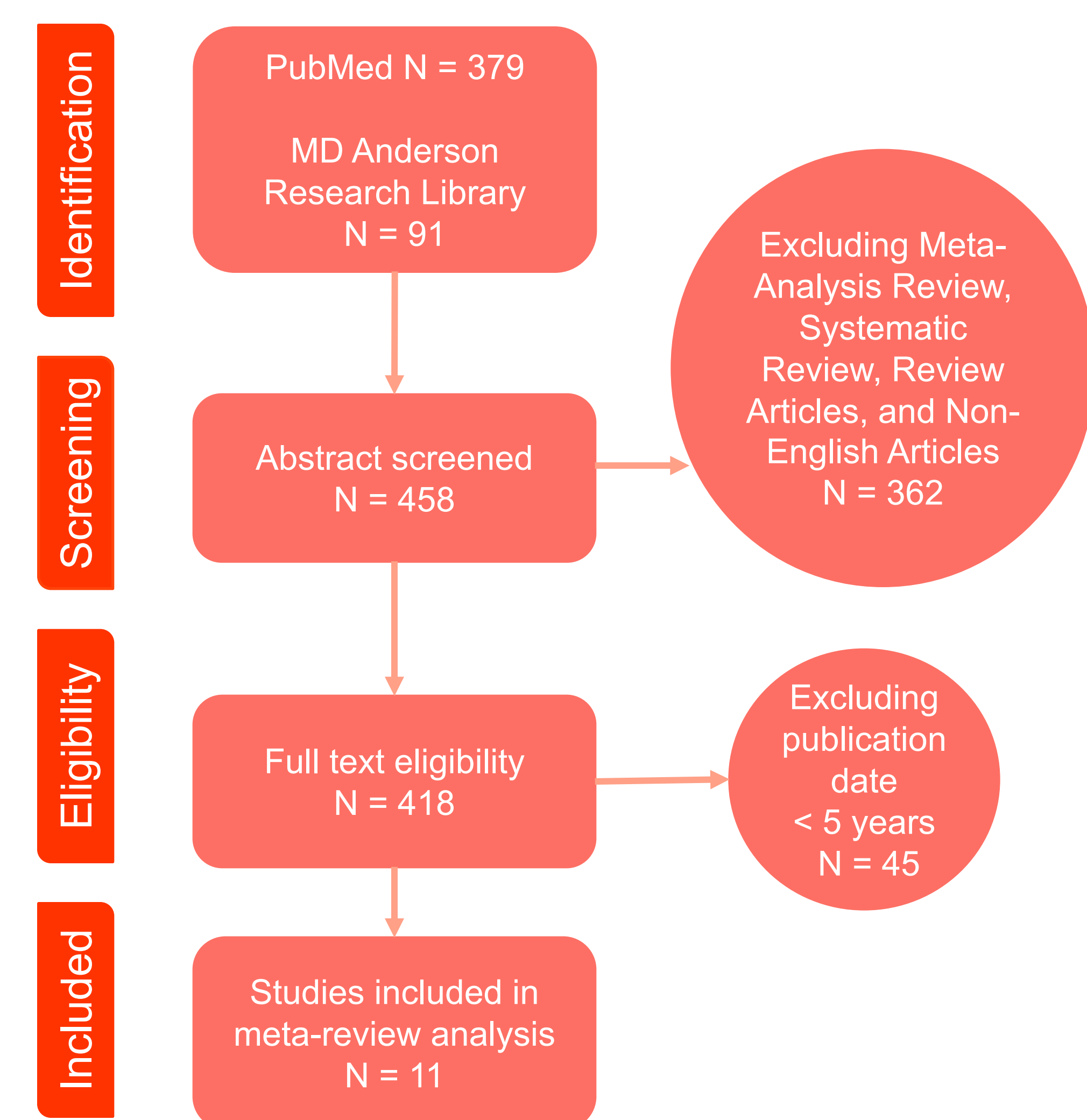
Can cold-stored platelets be used for emergency cases and be as effective as room-temperature platelets?

Methodology

A systematic search was done by screening through MD Anderson Research Library database and PubMed Database. The inclusion criteria included search terms: "cold-stored platelets + bleeding", "hemorrhage + cold-stored platelets", and "cold-stored platelets in trauma". The last day of research was February 17, 2024, and this included studies from 2019 – 2024.

Article Selection

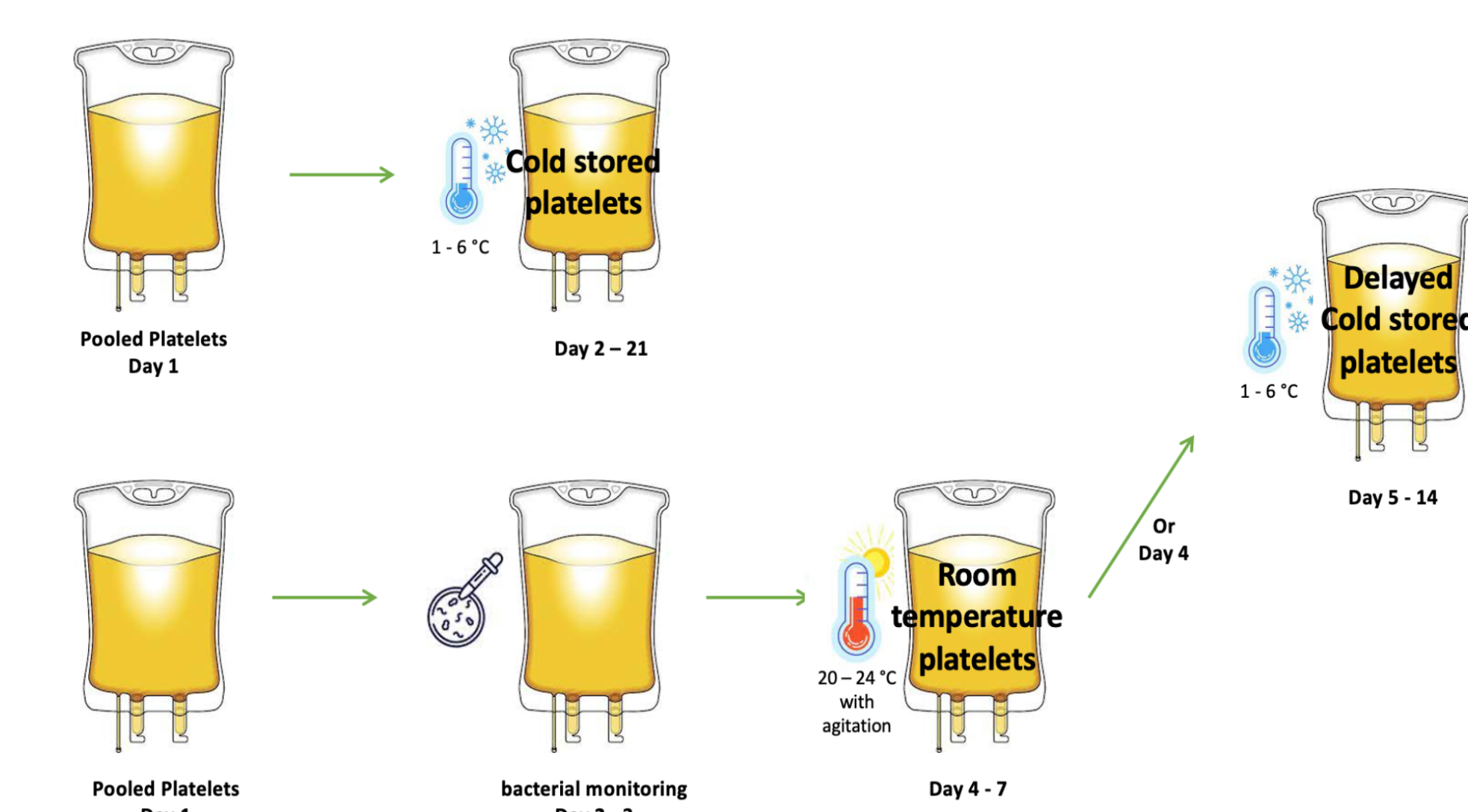
Figure 2. Flow Diagram of Selecting Articles



Note: Journal articles were screened through MD Anderson Research Library database and PubMed Database with keywords listed in the methodology. Articles only included primary articles with specific date ranges after the abstract screening and full-text eligibility, ending up with 11 eligible studies for a full meta-review analysis.

Key Findings

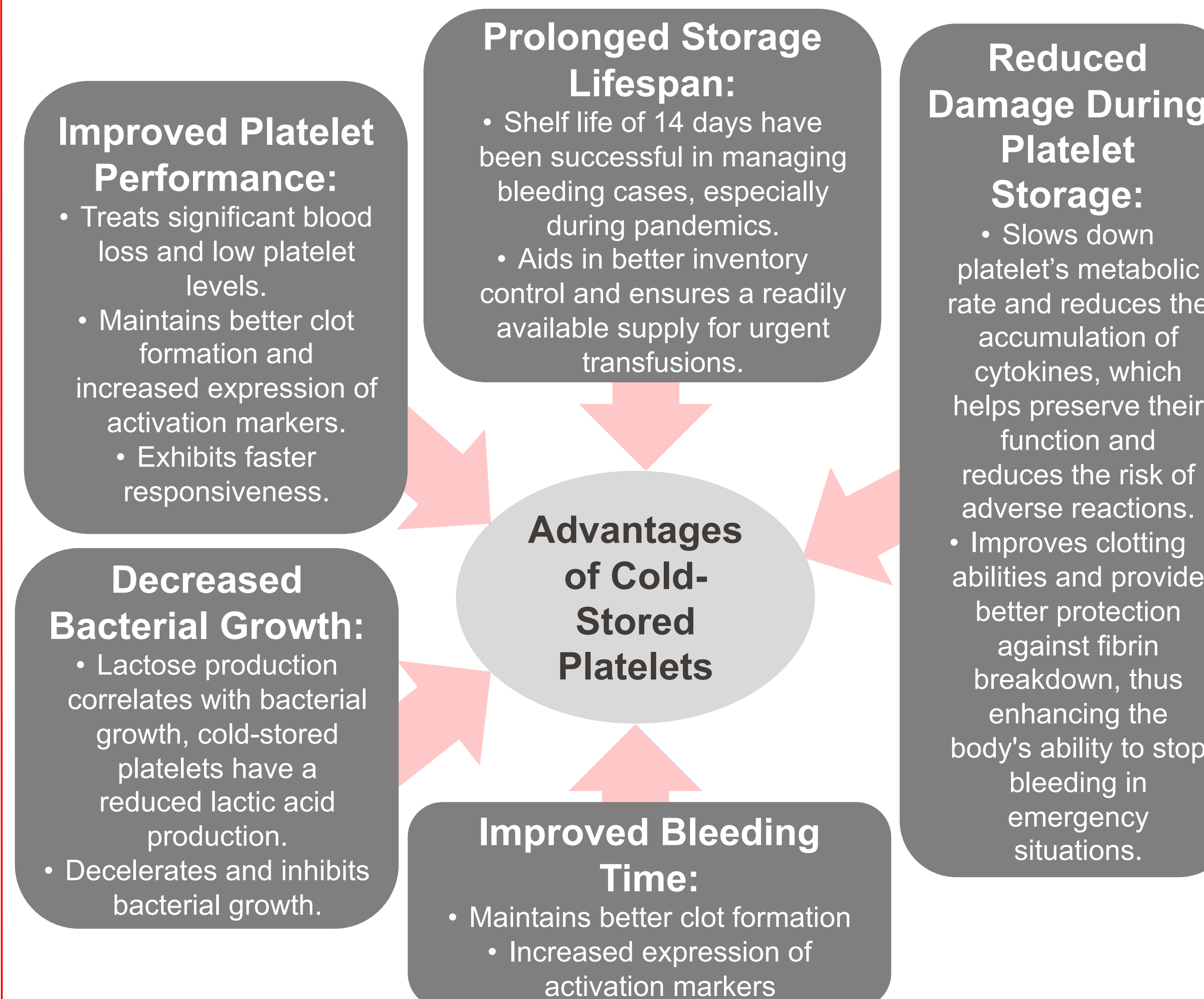
Figure 3. Process of Different types of platelet storage



Note: Article findings and research show that cold stored platelets can be functional for up to 21 days and are stored in the refrigerator at 1-6° C. Room temperature platelets must go through 2-3 days of bacterial monitoring and then stored on a platelet shaker with agitation at 20-24° C for up to 7 days. On day 4, platelets can be stored in refrigerated conditions for up to 14 days for functionality.

Results

Figure 4. Advantages of Cold-stored platelets



Strengths	Limitations
<ul style="list-style-type: none"> The review provides in depth insights into the uses and effects of cold-stored platelets (CSP) through detailed experimental design and thorough evaluation. The review also examines storage methods which directly enhances our understanding of how well CSP maintains platelet adaptability. 	<ul style="list-style-type: none"> Relies solely on lab settings and predetermined storage durations may restrict the practical application in real world scenarios. The small sample size and specific exclusion criteria could introduce bias, potentially limiting the generalizability of the findings. Little studies were found to have experiments conducted on examining the effects of cold-stored platelets in humans since the usage policy of cold-stored platelets was just recently passed.

Future Directions

Many of the studies experimented with CSP and RTP in vitro, providing evidence of how platelets react in the lab. With the passing of the FDA's approval of CSP, it is recommended to continue research on the effects of both types of platelets in vivo, studying pre and post transfusion data from human patients.

The goal is for the FDA to be able to extend their threshold of a maximum of 3 days storage of cold-stored platelets.

Conclusions

As of June 2023, the FDA has only approved storage of platelets for up to 3 days at 1-6° C for hemorrhage use and up to 14 days at 1-6° C for military use. For emergent platelet use, findings from the 11 primary studies showed that there is improved hemostasis and platelet aggregation within one-hour post-transfusion comparable to RTP. Although studies have shown that CSP are still functionally active at the 21-day mark, their hemostatic activity and platelet survival only lasts a few hours after transfusion (Braathen, 2022). Platelets that were delayed in cold storage showed no significant changes in platelet activation and were able to function comparable to CSP.

- Room temperature platelets are the most favorable when it comes to prophylactic treatments.
- Cold-stored platelets can provide a temporary solution to help with clotting factors in bleeding patients.

References

Apelseth, T.O., Doyle, B., Evans, R., George, C., Humbrecht, C., Klei, T., Tome Najdovski, Sigurjonsson, O. E., Wiltshire, M., & Dirk de Korte. (2023). Current transfusion practice and need for new blood products to ensure blood supply for patients with major hemorrhage in Europe. *Current Transfusion Practice and Need for New Blood Products to Ensure Blood Supply for Patients with Major Hemorrhage in Europe*, 63(S3).

Bjerkvig, C., Sivertsen, J., Braathen, H., Lunde, T. H. F., Strandenes, G., Assmus, J., Hervig, T., Cap, A., Kristoffersen, E. K., Fosse, T., & Apelseth, T. O. (2020). Cold-stored whole blood in a Norwegian emergency helicopter service: an observational study on storage conditions and product quality. *Transfusion*, 60(7), 1544–1551.

Braathen, H., Hagen, K. G., Kristoffersen, E. K., Strandenes, G., & Apelseth, T. O. (2022). Implementation of a dual platelet inventory in a tertiary hospital during the COVID -19 pandemic enabling cold-stored apheresis platelets for treatment of actively bleeding patients. *Transfusion*, 62(S1).

Braathen, H., Sivertsen, J., Lunde, T. H. F., Kristoffersen, E. K., Assmus, J., Hervig, T. A., Strandenes, G., & Apelseth, T. O. (2019). In vitro quality and platelet function of cold and delayed cold storage of apheresis platelet concentrates in platelet additive solution for 21 days. *Transfusion*, 59(8), 2652–2661.

Center for Biologics Evaluation and Research. (n.d.). Alternative procedures for the manufacture of cold-stored platelets. U.S. Food and Drug Administration.

George, C. E., Saunders, C. V., Morrison, A., Scorer, T., Jones, S., & Dempsey, N. C. (2023). Cold stored platelets in the management of bleeding: Is it about bioenergetics? *Platelets*, 34(1).

Huish, S., Green, L., Kempster, C., Smethurst, P., Wiltshire, M., Prajapati, C., Allen, E., & Cardigan, R. (2021). A comparison of platelet function in cold-stored whole blood and platelet concentrates. *Transfusion*, 61(11), 3224–3235.

Hulse, W., Bahr, T. M., Morris, D. S., Richards, D. S., Ilstrup, S. J., & Christensen, R. D. (2020). Emergency-release blood transfusions after postpartum hemorrhage at the Intermountain Healthcare hospitals. *Transfusion*, 60(7).

Kobsar, A., Koehnlechner, K., Klingler, P., Niklaus, M., Zeller-Hahn, J., Koessler, A., Weber, K., Boeck, M., & Juergen Koessler. (2022). The effect of short-term refrigeration on platelet responsiveness. *Scientific Reports*, 12(1).

Mack, J. P., Miles, J., & Stolla, M. (2020). Cold-stored platelets: Review of studies in humans. *Transfusion Medicine Reviews*, 34(4), 221–226 <https://doi.org/10.1016/j.tmr.2020.08.003>

Strandenes, G., Sivertsen, J., Bjerkvig, C. K., Fosse, T. K., Cap, A. P., del Junco, D. J., Kristoffersen, E. K., Haaverstad, R., Kvalheim, V., Braathen, H., Lunde, T. H. F., Hervig, T., Hufthammer, K. O., Spinella, P. C., & Apelseth, T. O. (2020). A Pilot Trial of Platelets Stored Cold versus at Room Temperature for Complex Cardiothoracic Surgery. *Anesthesiology*, 133(6), 1173–1183.

Warner, M. A., Kurian, E. B., Hammel, S. A., Buskirk, C. M., Kor, D. J., & Stubbs, J. R. (2020). Transition from room temperature to cold-stored platelets for the preservation of blood inventories during the COVID -19 pandemic. *Transfusion*, 61(1), 72–77.

Yang, J.-C., Liu, F.-H., Sun, Y., Ma, T., Xu, C.-X., Wang, W.-H., Chen, P., Xie, X.-X., Song, Y.-J., & Yin, W. (2019). Good hemostatic effect of platelets stored at 4°C in an in vitro model of massive blood loss and thrombocytopenia. *Medicine*, 98(18), e15454.

Zhao, H. Q., Serrano, K., Culibrk, B., Chen, Z., & Devine, D. V. (2022). Cold-stored platelets are effective in an in vitro model of massive transfusion protocol assessed by rotational thromboelastometry. *Transfusion*, 62(S1).